Barriers to Accepting &Completing Latent Tuberculosis Infection Treatment

Abstract:

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Abstract
Treatment of Latent Tuberculosis Infection (LTBI) is an important component of any TB control strategy. Acceptance and completion of treatment is poor. We undertook this study to identify barriers to acceptance & completion of treatment. Patients attending TB clinics completed a self-administered survey. Medical notes and electronic pharmacy records were reviewed. 143 surveys were completed. 70 (49%) completed treatment. Patients were less likely to accept treatment (p= 0.01, RR 0.781, CI 0.643-0.950) and less likely to complete treatment (p=0.01, RR 0.640, CI 0.462-0.885) when concerned about the side effects of LTBI medication. Completion of LTBI treatment is sub-optimal. The major barrier identified was fear about side effects caused by LTBI medications.

Introduction
Ireland has one of the lowest TB incidence rates in Western Europe with an average rolling incidence rate of 11/100,000 pop/year [1,2]. Treatment of Latent Tuberculosis Infection (LTBI) is an important component of any TB control strategy. In recent years, there has been an increase in the number of individuals considered to be at high risk for LTBI due to travel and migration [3]. Increasing rates of conditions such as HIV and treatment with immunosuppresants such as TNF-blockers have resulted in greater risk of progression from latent to active disease [4]. Other at-risk groups include diabetics, new tuberculin skin test converters, homeless and health care workers (HCWâ s). High-risk groups should receive priority treatment for LTBI [5]. However, rates of acceptance and completion of treatment are poor [6-9]. Our previous study reported that of 243 HCWâ s referred to the LTBI clinic, only 158 (65%) attended, 21% accepted and 13% completed treatment [6]. The reasons for non-acceptance and failure to complete treatment in our population, including non health care workers, have not been elucidated. The objective of this study was to identify the patientsâ views of LTBI and potential barriers to acceptance and completion of treatment.

Methods
The Patient Advocacy Committee has responsibility for approving surveys conducted in the hospital and gave approval for this study. Participation was voluntary. Consent was implied by completion of the questionnaire. Patients were recruited from two TB outpatient clinics in St James Hospital, Dublin (1) the LTBI clinic which receives referrals from the occupational health department, GPâ s or consultants and (2) the Public health clinic which provides a contact tracing service. An average 350 new patients are seen between both clinics annually. HIV+ patients with LTBI are seen in a different clinic, and were not included.
Screening at clinics consists of Mantoux test, chest x-ray, physical examination, medical history and baseline liver function test. A LTBI diagnosis was made in patients with a positive skin test (based on size listed in the Guidelines of the Prevention and Control of Tuberculosis in Ireland 2010) in the absence of any clinical or radiological evidence of active tuberculosis [5]. Unless contraindicated, all clinic attendees with LTBI were offered treatment. First line treatment provided was oral isoniazid 300mg daily for six to nine months. Standardised one to one verbal and written education regarding diagnosis, treatment, and side effects was provided. Patients were followed up monthly to six-weekly. Liver function tests were monitored and medications dispensed at clinic. Patients had access to the team by phone between visits. LTBI consultations, medication and tests are without charge. Patients were recruited between June 2008 and June 2010 using consecutive sampling. Treatment naive patients, 18 years or older, with a confirmed diagnosis of LTBI were included. Patients received their diagnosis and education and then were invited to complete the survey, regardless of their intention to accept or decline treatment. Patients were excluded from the study if they had a diagnosis of active TB, previous TB treatment or if isoniazid was contraindicated.

The first outcome measure was patient acceptance or refusal of LTBI treatment as recorded in the medical notes. The second outcome measure was patient views gathered by survey at the first clinic visit. The third outcome measure was completion of treatment, defined as taking 180 daily doses or more of isoniazid, which was recorded in the electronic pharmacy dispensing record and medical notes. A survey designed by Shieh et al, was adapted for the Irish healthcare setting [10]. The self administered survey comprises of 7 demographic questions and 21 multiple-choice questions relating to health beliefs, lifestyle, clinics and treatment regimens. The questionnaire was in English. Professional interpreters used in clinic could assist the patient in completion where required. All collected data were stored in Excel (Microsoft) database. R version 2.10.1 was utilised for analysis. Relative risks for acceptance of treatment and completion of treatment were calculated for groups agreeing/disagreeing with survey statements. 95% confidence intervals were constructed and univariate p-values obtained.

Results
Acceptance & Completion of LTBI Treatment
150 patients were approached, 5 refused, 2 surveys were incomplete and 143 surveys were completed. 101 of these patients (70%) accepted treatment. 70 (49%) patients completed treatment. In 16 cases treatment was stopped by a physician due to side effects and 12 patients failed to attend clinic after commencing treatment (Table 1).

Respondent Demographics & TB Risk Factors
Mean age 39.8 years (range 21 to 88 years). 64.3% of participants were female. 52% were HCWâ s, 43% were born in a TB endemic country, 24% were recent contacts of active TB cases and 17% were due to commence biological agents (Table 2). Demographics such as gender (p= 0.725), social class (p= 0.225), country of birth (p=0.328) or ethnicity (p= 0.300) did not influence the participantsâ decision to accept or decline treatment. However, the patientâ s occupation and risk factors did show a trend towards having a statistically significant influence on accepting or declining treatment. Hospital workers were less likely to accept treatment (p= 0.067) whereas patients due to commence biological agents were more likely to accept treatment (p=0.096).

Perceived Barriers
Participants had good general knowledge about LTBI. 85% believed that there was a chance that this could wake up and make them sick and 90% of participants believed that the LTBI treatment would kill the LTBI in their lungs. Life style and clinic arrangements such as travelling time and expenses, frequency of appointments, times and duration of visits, taking time off work or college were not identified as barriers to treatment. Elements of the treatment regimen such as being unable to take paracetamol or alcohol and the need for venepuncture were not identified as barriers. However, participants were less likely to accept LTBI treatment (p= 0.01, RR 0.781, CI 0.643-0.950) and less likely to complete LTBI treatment (p=0.01, RR 0.640, CI 0.462-0.885) when concerned about the side effects of LTBI medication (Table 3).

Discussion
This paper reports the barriers to accepting and completing LTBI treatment. 70% of those recommended to start treatment commenced it, a result similar to other health centres [8,11]. But less then 50% of those advised to commence treatment went on to complete it. HCWâ s were less likely to accept treatment, whereas patients due to commence biological agents were most likely to accept treatment. The main barrier to accepting and completing LTBI treatment was the fear of side effects. The standard treatment of LTBI is isoniazid therapy for 6 to 9 months. This is fraught with evidence of poor compliance which is particularly worrying in HCWâ s whose risk of reactivation poses a potential risk of nosocomial exposure to tuberculosis. Many of these HCWâ s were recruited from countries with high TB prevalence. Screening and treating hospital staff is important. In 2002, 4% of TB cases in New York were in HCWâ s, an increase from 2.5% in 1994 even though overall TB rates had declined. Of the HCWâ s with TB, nearly 60% had positive Mantoux at the start of employment, but the majority did not receive prophylaxis treatment [12].

HCWâ s in our study had the lowest treatment acceptance rate (63%). Many of our HCWâ s were young female nurses. Kwara et al found that pregnant women or those planning to become pregnant were less likely to accept and adhere to treatment [13]. Family planning may have contributed to the lower acceptance rate, although we did not find a statistically significant association with gender. Furthermore, HCWâ s might have the opinion that their positive mantoux is a result of past BCG vaccination i.e. a â false positiveâ and opt out of treatment. 35% of those vaccinated at an older age can have a BCG related positive mantoux test [14,15]. The use of Interferon-Gamma Release Assays (IGRA) in addition to mantoux testing has been recommended in the diagnosis of LTBI because IGRA has a higher specificity and is unaffected by prior BCG vaccination [16,17].

HCWâ s also had the lowest completion rate (42%). One explanation offered is that this group may never have intended initiating treatment but were unwilling to refuse the offer of treatment [11]. This may be particularly relevant when being treated in the hospital they also work in. Of the 12 participants who failed to attend clinic after commencing LTBI treatment, 7 of these were HCW's. This may be explained by their unwillingness to refuse treatment, however the multitude of reasons why patients fail to attend appointments cannot be extrapolated from this study. Patientsâ perception of the degree of risk of developing TB can influence their decisions [10]. Patients commencing immunosuppressive biological agents were the most likely to accept and complete treatment. Their risk of reactivation of LTBI is 10 to 20 per cent after commencing biological agents [18]. This higher risk may have resulted in their willingness to take treatment, additionally awareness that treatment with biological agents may be denied, if they refuse LTBI treatment. Twenty two of the 25 patients in this cohort accepted treatment and 1 failed to attend clinic after commencing LTBI treatment. Biological agents were withheld in all patients who did not complete treatment.

Frequently it is assumed that health beliefs differ among and are influenced by ethnicity and demographics. Demographic associations with acceptance and completion of LTBI treatment have varied between studies [10,11,13,19]. Despite the diverse demographics of the participants in the study, neither, social class nor ethnicity influenced their decision to accept or decline treatment. The chief finding identified in our study is that patients who were concerned about treatment side effects were less likely to accept and complete treatment. Preventative measures at the clinic were in line with American Thoracic Society guidelines. Despite the incidence rate of isoniazid related hepatitis being only 1 in 1000, patients still had concerns about side effects outweighing the benefits of treatment [20]. Treatment was stopped due to side effects in 16 patients; these included elevated transaminases, peripheral neuropathy, GI upset and all reversed on cessation of therapy (Table 1). In each case the physician, in conjunction with the patient, made a decision to stop isoniazid therapy as the risk of the adverse event outweighed the benefit of continuing to treat LTBI. Published data demonstrate that 10% to 20% of persons taking isoniazid will have some mild, asymptomatic elevation of liver enzymes [21]. Other factors such as giving up alcohol, venepuncture, knowledge and information about TB, were not significantly associated with treatment completion. Our findings differ from those reported by Shieh, where concern about venepuncture was an identified barrier [10]. A focus group of HCWâ s in the US did identify adverse events as a barrier to taking LTBI treatment [9]. The fear of side effects of medication is a genuine concern.

The option to take a shorter course may be more attractive for patients. Adherence is better with 4 month rifampicin course compared to isoniazid [22]. Rifapentine plus isoniazid once weekly for 3 months has been shown to be as effective as 9 months of isoniazid [23]. Additionally it had a higher completion rate albeit directly observed therapy was utilised. The population studied was heterogeneous, this reflects the TB clinic population. It was unrealistic to cohort

patients as the numbers in each category would be small and have weak statistical results. The patient population was heavily weighted to HCWâ s. Their views may not be representative of all patients. However, they are a substantial population of LTBI patients for whom treatment is recommended. Completion of LTBI treatment is sub-optimal, even in a population that includes health care workers and high-risk individuals. The causal reasons for non-acceptance and non-completion of treatment are multifactorial. However this study found that fear of side effects stopped patients accepting or completing treatment. We need to support patients from decision making to the end of treatment, with the availability of IGRA, side effect information and shorter treatment regimens.

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